

**REMARKS**

Reconsideration of this application, as amended, is respectfully requested. Claims 1, 2 and 4-27 were pending in this application. New claims 29-31 have been added with this amendment. This amendment does not add any new matter. Applicants reserve the right to prosecute any unclaimed or cancelled subject matter in this or another application as appropriate. Consideration and entry of this amendment is respectfully requested.

**REJECTIONS UNDER 35 U.S.C. 103(a)****A. Claims 1, 2, 4-17 and 20**

Claims 1-2, 4-17 and 20 stand rejected under 35 U.S.C. 103(a) over Hurpin (1998) in view of Hodge (1997), Rice (US Pat. No. 6,127,116; 1997), and Lehner (1999). Applicants respectfully traverse these rejections as indicated below.

In this rejection, the Examiner first reminds Applicants that the rejection is based on the combined teachings of Hurpin, Hodge, Rice and Lehner and that attacking the references individually is improper as the rejection is based on a combination of the references. Applicants do not disagree with the Examiner's characterization of the case law and have pointed to the deficiencies in each reference individually to emphasize that the combination is defective and cannot render the instant claims obvious.

The Examiner cites Hurpin, Hodge, Rice and Lehner as providing the motivation to immunize patients in a prime-boost format where antigen is directly administered into a lymph node. Hurpin is cited for providing motivation to immunize through a lymphatic route as intrasplenic administration of ALVAC p53 is shown to be immunogenic and that certain prime-boost methods may be useful. Hodge is cited for providing the motivation to use a diversified prime-boost protocol through the demonstration of a vaccinia-ALVAC prime-boost methodology. Rice is cited for providing motivation to administer antigen directly into a lymph node. Lehner is also cited for providing motivation to deliver antigen to a lymph node. Applicants respectfully disagree that these references together would have suggested to one of skill in the art that one could (with any reasonable expectation of success) administer antigen directly to a lymph node and achieve an improved immune response.

The Examiner's rejection points only to Lehner as providing the requisite reasonable expectation of success. However, as Applicants have previously pointed out, Lehner teaches "a subcutaneous immunization technique, which aims to administer the vaccine in the proximity of the internal and external iliac lymph nodes...." (Lehner, p. S489, col. 2). Applicants respectfully disagree that Lehner's disclosure would have provided the skilled artisan with a reasonable expectation of success that direct intranodal administration would induce or enhance an immune response.

Applicants' specification provides a comparison of a subcutaneous route of administration "in the proximity" of lymph nodes to the claimed method. Antigen was administered subcutaneously in the dorsal cervical / "intercapsular" (i.e., intracapsular) regions (known to contain lymph nodes) and compared to administration directly into the left inguinal lymph node. As shown in Applicants' Figure 5, direct intranodal administration resulted in a much greater immune response than that following subcutaneous administration; the data shows that immune response following subcutaneous administration was comparable to that of the saline control. Thus, Applicants' method induced a strong immune response while a method arguably similar to that of Lehner did not. In order to show a reasonable expectation of success, the Examiner must show that the results would have been at least "reasonably predictable" ("Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.*", Fed. Reg. 72 (195), Oct. 10, 2007). It is known that the field of vaccines is highly unpredictable. As shown in the specification, even a method similar to Lehner's lacks reasonable predictability. If, as the Examiner alleged, one would have predicted Applicants' method to be predictable from Lehner (in combination with the other cited references), one certainly would have expected the results of experiments similar to Lehner's to be predictable. But the specification shows this not to be the case. Applicants respectfully maintain that it was not until the Applicants actually carried out the experiments that the skilled artisan had any reasonable expectation of success in successfully using direct intranodal vaccination.

The methods of the cited art and those instantly claimed are different and part of a highly unpredictable art. Applicants respectfully disagree with the Examiner's

conclusions that the claimed invention was obvious in view of the cited art. Accordingly, it is respectfully requested that these rejections be withdrawn.

**B. Claims 18-19**

Claims 18 and 19 stand rejected under 35 U.S.C. 103(a) over Hurpin (1998) in view of Hodge (1997), Rice (US Pat. No. 6,127,116; 1997), and Lehner (1999) as applied to claims 1-2, 4-17 and 20 and further in view of Zaremba (1997) and Salgaller (1996). Applicants respectfully traverse these rejections as indicated below.

Applicants have discussed the deficiencies of the references as applied to claims 1-2, 4-17 and 20 above. Applicants do not believe that the cited references provide any reasonable expectation of success or any reasonable predictability in carrying out the claimed methods. Thus, as described above, Applicants respectfully disagree with the Examiner's position with respect to claims 1-2, 4-17 and 20. Applicants maintain their position in responding to these rejections. Hurpin, Hodge, Rice and Lehner do not render claims 1-2, 4-17 and 20 obvious; as such, the rejection of dependent claims 18 and 19 on the same reasoning is improper. Applicants do not believe either Zaremba or Salgaller satisfy the deficiencies in the rejection of claims 1-2, 4-17 and 20 (as described above). Accordingly, it is respectfully requested that these rejections be withdrawn.

**C. Claims 21-27**

Claims 21-27 stand rejected under 35 U.S.C. 103(a) over Hurpin (1998) in view of Hodge (1997), Rice (US Pat. No. 6,127,116; 1997), and Lehner (1999) as applied to claims 1-2, 4-17 and 20 and further in view of Barnett (1997). Applicants respectfully traverse these rejections as indicated below.

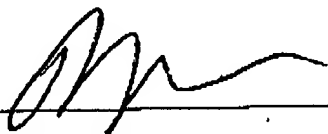
Applicants have discussed the deficiencies of the references as applied to claims 1-2, 4-17 and 20 above. Applicants do not believe that the cited references provide any reasonable expectation of success or any reasonable predictability in carrying out the claimed methods. Thus, as described above, Applicants respectfully disagree with the Examiner's position with respect to claims 1-2, 4-17 and 20. Applicants maintain their position in responding to these rejections. Hurpin, Hodge, Rice and Lehner do not render claims 1-2, 4-17 and 20 obvious; as such, the rejection of dependent claims 21-27 on the

same reasoning is improper. Applicants do not believe either Barnett satisfies the deficiencies in the rejection of claims 1-2, 4-17 and 20 (as described above). Accordingly, it is respectfully requested that these rejections be withdrawn.

### CONCLUSIONS

Consideration and entry of this response is respectfully requested. Applicants believe the claims are now in condition for allowance, and respectfully request that a Notice of Allowance be issued as soon as possible. The Examiner is encouraged to contact the undersigned if it is believed doing so would assist in the examination of this application.

Date: October 31, 2007



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